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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
KOLKER, DANIEL E	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 10/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,575	SCHENK, DALE B.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,58 and 74-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,58 and 74-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/5/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's remarks and amendments filed 5 August 2005 have been entered. Claims 11, 58, 74 – 81 are pending and under examination.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejections and Objections

3. The following rejections and objections made in the previous office action are withdrawn:

The objection to claim 11 is withdrawn in light of applicant's amendment.

The rejection of claims 11 and 58 under 35 USC 112, first paragraph for lacking written description is withdrawn in light of applicant's arguments.

New Rejections

Priority

4. 35 U.S.C. § 120 states that:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

35 U.S.C. § 119(e) states that:

> An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

5. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 120 or § 119(e) from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention.

There is no disclosure or contemplation of administration of antibodies which bind to synuclein-NAC in application 09/580,015 or 09/322,289 or 09/201,430. Thus claims which

recite such administration, i.e. all pending claims, only receive priority to the date that such administration was contemplated, namely the date that parent application 09/585,817 was first filed, 1 June 2000.

Should applicant disagree with the factual determinations above, applicant should supply evidence that the previous applications do in fact constitute enabling disclosures. This could be accomplished, for example, by directing the examiner's attention to specific page and line numbers in previous applications where such support can be found.

Claim Rejections - 35 USC § 112

6. Claims 11, 58, and 74 – 81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administration of chimeric, humanized, or human antibodies which specifically bind to the non-amyloid component of alpha synuclein and chimeric, humanized, or human antibodies that specifically bind to residues 1 – 28 of A-beta, does not reasonably provide enablement for therapeutic or prophylactic treatment of Alzheimer's disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

In the instant case the nature of the invention, treatment of Alzheimer's disease, is complex. The specification does not disclose working examples in which therapeutic treatment of Alzheimer's disease has been accomplished. Alzheimer's disease is characterized by loss of memory (see for example Small et al. 2000. Proc Natl Acad Sci USA 97:6037-6042), thus therapeutic treatment of Alzheimer's disease would necessarily have to show reduction of the severity or frequency of symptoms in patients afflicted with the disease. In the absence of disclosure of actual alleviation of symptoms by the claimed method, claims to "therapeutic treatment" cannot be considered fully enabled.

Similarly, the art recognizes that prophylactic treatment of Alzheimer's disease is essentially impossible. While several terms are explicitly defined on pp. 11 – 15 of the specification, "prophylactic" is not among them. Thus the term is given its common meaning within the art, as indicated by applicant (specification, p. 11, lines 2 – 3). The attached printout for "prophylactic" from www.dictionary.com shows that several dictionaries, including both The American Heritage Dictionary (2000), and Stedman's Medical Dictionary (1995 – 2002) include prevention within the scope of the definition. In order for claims drawn to prophylactic administration of the antibodies to be considered enabled, the specification would have to disclose prevention of Alzheimer's disease in patients susceptible to it. However there is no disclosure of prevention of Alzheimer's disease. The example which appears on p. 105 drawn to prevention is prophetic in nature. Therefore claims to "prophylactic treatment" cannot be considered fully enabled.

While there is disclosure of treatment of PDAPP mice by administration of antibodies against beta-amyloid (specification, p. 83 – 84 and 95 – 105) the specification does not disclose the results of experiments wherein antibodies to NAC decrease the severity of Alzheimer's disease symptoms in either human patients or an art-recognized model. Page 115 of the specification discloses that antibodies against NAC can be used to reduce plaques *ex vivo*, but since the *ex vivo* assay is not a reliable model of Alzheimer's disease it does not constitute disclosure of either therapeutic or prophylactic treatment of the disease. Furthermore the specification does not disclose which regions of NAC served as the antigen, the specificity of the antibody, or whether or not it is a chimeric, human, or humanized antibody. Finally, as independent claims 11 and 58 recite "synuclein-NAC" but the art recognizes that only a portion of the alpha synuclein protein is involved in Alzheimer's disease (see Clayton 1999. Journal of Neuroscience Research 58:120-129, particularly Figure 1), antibodies which bind to other portions of alpha synuclein, or to other synucleins, would not be expected to be successful in either therapeutic or prophylactic treatment.

7. Claims 11, 58, and 74 – 81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Independent claims 11 and 58 recite "synuclein-NAC". This term is not explicitly defined in the specification. The claims are drawn to methods comprising administering antibodies which specifically bind to "synuclein-NAC". There are several known synucleins; Clayton (1999. Journal of Neuroscience Research 58:120-129) teaches that at least three were known before the time of invention however only one, alpha synuclein, was known to be involved in neurodegenerative diseases. Furthermore Clayton teaches that NAC is a portion of alpha synuclein but NAC does not appear to be part of the other (beta and gamma) synucleins. The specification discloses antibodies raised against NAC (see p. 115) but there is not disclosure of the instantly-claimed method using antibodies raised against either other synucleins or against the domain which corresponds to NAC in either beta or gamma synuclein.

The instant disclosure of a single antibody which binds to the NAC domain of alpha synuclein, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

As the specification only discloses a single antibody which binds to part of one synuclein, there is not sufficient disclosure to support the claimed methods, which include antibodies which bind to any of the synucleins. As the synuclein proteins differ considerably (see Clayton for a more detailed description), an antibody which binds to one of the synucleins would not necessarily be expected to bind to the others.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 11, 58, 74 – 75, and 78 – 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Masliah (WO 95/06407, published 9 March 1995) and Schenk (U.S. Patent 6,710,226, issued 23 March 2004, filed 27 November 2000, claiming priority to provisional applications filed 2 December 1997 and 7 April 1998), or in the alternative over Masliah and Schenk (WO 99/27944, published 10 June 1999). Applicant is advised that the '226 patent appears to have an identical disclosure to that of the '944 publication. The text below refers to specific column and line numbers from the U.S. Patent.

Masliah teaches treatment of Alzheimer's disease by administration of "NAC peptides" (see p. 50 lines 12 – 22). The scope of the term "NAC peptides" is provided on p. 22 of Masliah as those peptides which "will specifically bind NAC *in vivo*; the peptides will, therefore, have at least one binding site for NAC." (p. 22, lines 16 – 20). Masliah also teaches how to make anti-NAC antibodies in general (see p. 36 line 11 – p. 38 line 23) and chimeric antibodies in particular (see p. 38 lines 1 – 5; while Masliah does not use the word "chimeric" he teaches genetically engineered antibody constructs including CDR grafted antibodies, which fall within the scope of the very broad usage of the term "chimeric antibodies" provided on p. 37 of the specification), thereby guiding the artisan of ordinary skill to select chimeric antibodies as the NAC peptide for therapeutic administration. Masliah teaches administration by several routes including epidural, intralumbar, and intrarterial (p. 54 lines 6 – 11) and pharmaceutical compositions comprising carriers (p. 58 line 11 – p. 59 line 8). Masliah also claims the antibodies (see claims 21 – 23) and methods of treating amyloid disorders, including those characterized by formation of neuritic plaques by administering antibodies against NAC (see for example claims 48, 51 – 52, 56, 58 – 59, and 62). The artisan of ordinary skill would immediately recognize that this includes Alzheimer's disease, which is characterized by neuritic plaques and in fact Masliah explicitly teaches Alzheimer's disease can be treated by the disclosed methods (see p. 50 lines 12 – 22). Masliah does not teach co-administration of the antibodies with chimeric, humanized, or human antibodies which bind to an epitope within

residues 1 – 28 of A-beta. As the definition of "prophylactic" includes slowing the spread of disease (see printout from dictionary.com, final page) and the methods of Masliah are for decreasing the severity of the symptoms, the prior art also applies to "prophylactically treating" as recited in claim 58.

Schenk teaches both prophylactic and therapeutic treatment of Alzheimer's disease by administration of chimeric, human, and humanized antibodies which bind to epitopes within residues 1 – 28 of A-beta (see column 2 lines 18 – 38). Schenk also teaches pharmaceutical compositions comprising carriers (column 22 lines 18 – 38), various routes of administration including oral, topical, subcutaneousl, intraperitoneal, intramuscularly, and intranasal (column 20 lines 35 – 40) and intravenous (column 2 line 46). Further Schenk teaches sustained release compositions (column 23 lines 5 – 11) and treatment via multiple dosages for at least six months (column 2 lines 29 – 46).

It would have been obvious to one of ordinary skill in the art to co-administer antibodies from Maslaih and Schenk, with a reasonable expectation of success. Co-administration of two compounds each known to be effective for the same purpose is *prima facie* obvious and flows logically from the prior art. See MPEP § 2144.06.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel E. Kolker, Ph.D.
October 13, 2005

SHARON TURNER, PH.D.
PRIMARY EXAMINER
10-13-05